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Effect of preoperative HbA1C levels on postoperative acute renal failure in diabetic patients undergoing coronary bypass surgery

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ABSTRACT

Introduction: Open heart surgery in patients with diabetes mellitus (DM) is associated with a higher mortality and morbidity than other patients. Diabetes mellitus (DM) is present in 30 to 40% of patients undergoing coronary bypass surgery (CABG). In this study, we aimed to clarify the relationship between preoperative glycohemoglobin (HbA1C) levels and postoperative acute renal failure (ARF) in patients with DM undergoing isolated coronary bypass surgery. *Methods:* We retrospectively enrolled a total of 295 patients who underwent elective, isolated CABG between January 2014 and February 2017 in our clinic and whose information was recorded. DM was detected in 118 of 295 patients. These patients were divided into two groups as Group 1 (HbA1c levels <7%, n = 72) and Group 2 (HbA1c levels >7%, n = 46). All patients were treated with standard insulin therapy after consulting the internal medicine department before the operation. *Results:* Of the 118 patients included in the study, 82 were males and 36 were females. There were 72 patients (51 M, 21 F) in Group 1 and 46 patients (31 M, 15 F) in Group 2. The mean age was 62.4 ± 3.2 years in Group 1 and 61.5 ± 4.5 years in Group 2. The mean duration of DM diagnosis was 10.2 ± 3.3 years in Group 1 and 11.7 ± 2.6 years in Group 2. The mean duration of hospitalization in intensive care unit was 6.10 ± 2.3 days in Group 1 and 9.1 ± 2.5 days in Group 2, which was found to be statistically significant (p=0.008). *Discussion and conclusion*: Hemodialysis (HD) may be required after coronary bypass surgery in diabetic patients. Although there is no direct correlation between high HbA1c levels and postoperative HD, we believe that these patients should be more closely monitored with more frequent measurements of urea, creatinine, blood gas and electrolyte levels.

Keywords: Diabetes mellitus, Hemodialysis, glycohemoglobin, creatinine

1. INTRODUCTION

Diabetes mellitus (DM), which is one of the biggest diseases of our age, has an incidence of 5 to 10% in developed societies (Guariguata et al., 2014). Of these, 90 to 95% have type 2 DM. The remaining 5 to 10% have type 1 DM. This disease is the most important cause of blindness, chronic kidney failure (CRF), non-traumatic amputations in the community (Huang et al., 2014). DM has been associated with a 4-fold increase in the risk of cardiovascular diseases. DM becomes a disease with increasing prevalence with aging with risk factors such as genetic factors, poor, irregular and fast food eating habits and stressful conditions (Michael et al. 2010). This increase has an adverse effect on the economy. Given the complications in diabetic patients in particular, this adverse effect on the economy can reach enormous size. Therefore, it is possible to reduce costs due to these complications by raising the awareness of patients about health services and especially DM.

Despite improvements in technical equipment and experience in coronary bypass surgery, mortality rate remains still at the level of 3 to 5% (Verma et al., 2013). Among these mortalities, ARF due to renal injury has an incidence of 30% in cardiopulmonary bypass surgery (Karakan et al., 2012). Therefore, DM accounts for 2 points in the EUROSCORE risk-scoring system. Postoperative blood urea nitrogen (BUN) and creatinine levels may be elevated in DM patients undergoing coronary bypass surgery, which is often transient and tends to decrease with appropriate fluid electrolyte treatment on subsequent days. However, in some patients, BUN and creatinine levels increase and urine output decreases during the follow-up period. Mortality and morbidity rates are increasing unless urgent intervention is provided in these patients.

In this study, we aimed to investigate the relationship between preoperative HbA1c levels and HD due to ARF after CABG surgery.

2. MATERIALS AND METHODS

The study protocol was approved by the YüzüncüYıl Universty Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki. We retrospectively enrolled a total of 295 patients who underwent elective, isolated CABG between January 2014 and February 2017 in our clinic and whose information was recorded. DM was detected in 118 of 295 patients. Patients with low cardiac output, acute or chronic renal failure, chronic obstructive pulmonary disease, a history of myocardial infarction, preoperative arrhythmia, and who underwent emergency surgery, additional surgery, ascending and thoracic aortic surgery and additional valve surgery were excluded from the study. Additionally non-diabetic patients were excluded from the study. These patients were divided into two groups as Group 1 (HbA1c levels <7%, n = 72) and Group 2 (HbA1c levels >7%, n = 46). All patients were treated with standard insulin therapy after consulting the internal medicine department before the operation. The

study included 118 patients with diabetes mellitus aged 38 to 77 years who underwent elective CABG. During the preoperative period, all patients were hospitalized for 3 days and consulted to departments of internal medicine, chest diseases and anesthesia and reanimation, and the blood glucose levels of the patients were measured 4 times a day. The patients were subjected to respiratory function tests, complete blood count and measurement of biochemical and coagulation parameters and body mass index (BMI). Prior to the operation, all patients were premedicated with 0.07 mg/kg dormicum and 20 mcg/kg atropine. Patients underwent routine coronary artery anesthesia. Standard and invasive monitoring was performed for this purpose. Heart rates (ECG) and arterial saturation (SpO_2) and central venous pressure (CVP) values of the patients were monitored. Anesthesia induction was achieved with propofol 1 mg/kg, midazolam 0.1 mg/kg/IV, fentanyl 0.8 µg/kg/IV and esmeron 0.7 mg/kg/IV. The patients were mechanically ventilated after the intubation with a maintenance infusion of sevoflurane and fentanyl (7 µg/kg/h) in a 0.5:0.5 mixture of air and oxygen.

In all patients, the left internal mammary artery (LIMA) graft was used for the revascularization of the left anterior descending artery (LAD).Intraoperative variables such as number of distal anastomoses, use of inotropic agent, CPB duration (minutes) and cross clamp duration (minutes) were recorded and evaluated.

Intraoperative CPB, aortic cross clamp and intubation durations, follow up of blood gases and urine, and postoperative hemodynamic parameters, daily serum BUN and creatinine values and amount of drainage were recorded. Patients with creatinine values of 2.5 and above, BUN values of 100 and above, decreased urine output and impaired blood gas and hemodynamic parameters were considered as ARF and hemodialyzed.

Statistical analysis

Data were analyzed with SPSS (Version: 17.0) package program (Statistical Package for the Social Sciences, Chicago, IL, USA). Descriptive statistical methods (Frequency, Percentage, Mean, Standard deviation) were used in the evaluation of the data. In addition, Mann-Whitney U test was used for intergroup comparisons. The Wilcoxon sign test was used for intra-group comparison of creatinine and BUN parameters. The results were evaluated at 95% confidence interval with a significance level of $p < 0.05$.

3. RESULTS

Of the 118 patients included in the study, 82 were males and 36 were females. The mean age of these patients was 61.5 ± 3.2 years. The mean age of the patients was 63.5 ± 4.2 years in males and 57.2 ± 3.1 years in females. There were 72 patients (51 M, 21 F) in Group 1 and 46 patients (31 M, 15 F) in Group 2. The mean age was 62.4 ± 3.2 years in Group 1 and 61.5 ± 4.5 years in Group 2. The mean duration of DM diagnosis was 10.2 ± 3.3 years in Group 1 and 11.7 ± 2.6 years in Group 2. Type 1 and 2 DM were found in 5 (6.9%) and 67 (93.1%) patients, respectively, in 72 patients in Group 1, and 6 (13.1%) and 40 (86.9%) patients, respectively, in Group 2. Five patients with Type 1 DM in Group 1 received standard insulin therapy, whereas of the patients with Type 2 DM, 52 received oral antidiabetic therapy (OAT) and 15 received OAT and insulin therapy. Two patients with Type 1 DM in Group 2 received standard insulin therapy, whereas of the patients with Type 2 DM, 35 received oral antidiabetic therapy (OAT) and 5 received OAT and insulin therapy. Preoperative demographic data of the patients are given in Table 1. There was no statistically significant difference between groups in terms of smoking habit, COPD (p=0.710) and HT (p=0.660). The mean duration of aortic cross clamping (ACC) was 53.6 ± 26.1 minutes in Group 1 and 58.6 ± 15.3 minutes in Group 2. Preoperative, peroperative, and postoperative fasting blood glucose levels of the patients were 161±46 mg/dl, 214±58 mg/dl and 142±65 mg/dl in Group 1 and 193±34 mg/dl, 246 ± 68 mg/dl and 198±59 mg/dl in Group 2, respectively. The mean number of distal anastomoses was 2.1 ± 0.9 in Group 1 and 2.1 ± 0.6 in Group 2 and did not show statistically significant difference (p=0.650). Intraoperative results are presented in Table 2.

Postoperative acute renal failure was diagnosed according to RIFLE (Risk, Injury, Failure, Loss, ERDS) within the first 7 days. Hemodialysis was started with classical jugular or femoral venous dialysis catheter after nephrology consultation for our patients. Hemodialysis was required in 4 of the patients in Group 1 (5.5%) and 11 of patients in Group 2 (23%), which was found to be statistically significant ($p < 0.05$). The rate of mortality was %2.7 (n=2) in non-hemodialysis patients and 1.3% (n=1) in hemodialysis patients in Group 1, whereas 4.3% (n=2) in non-hemodialysis patients and 4.3% (n=2) in hemodialysis patients in Group 2 (p=0.001). The mortality rate of non-hemodialysis patients was attributed to low cardiac output and pulmonary infections. The mean duration of hospitalization in intensive care unit was 6.10 ± 2.3 days in Group 1 and 9.1 ± 2.5 days in Group 2, which was found to be statistically significant (p=0.008).Postoperative results are presented in Table 3 and HbA1c ratios according to age distribution are presented in figure 1.

Table 1 Preoperative Patient Information

Variable	Group 1 (n = 72)	Group 2 (n = 46)	p value
Mean age (years)	62.4 ± 3.2	61.5 ± 8.3	0.232
Gender (Male/Female)	51 M/21 F	31 M/15 F	0.398
Duration of diagnosis of DM (years)	10.2 ± 3.3	11.7 ± 2.6	0.328
Mean BMI (kg/m^2)	24.3 ± 4.8	25.2 ± 2.1	0.118
Past history of MI (%)	35 (48.6%)	21 (45.7%)	0.312
Mean EF (%)	41 ± 5.8	44 ± 3.6	0.530
Use of Acetyl Salicylic Acid n (%)	55 (76%)	32 (69%)	0.240
Hypertension n (%)	65 (90.2%)	40 (86.9%)	0.660
Chronic Obstructive Pulmonary Disease n (%)	15 (20.8%)	10 (21.7%)	0.710
Smoking n (%)	23 (31.9%)	18 (39.1%)	0.580
Mean blood glucose level (mg/dL)	161 ± 46	193 ± 34	0.730
Serum creatinine level (mg/dl)	1.1 ± 0.98	0.9 ± 1.13	0.460
Serum urea level (mg/dl)	35 ± 3.6	38 ± 4.1	0.670
Hemoglobin level (gr/dl)	12 ± 2.4	13 ± 1.5	0.770
INR	1.3 ± 0.32	1.2 ± 0.42	0.320
Platelet level	186,000 ± 25,000	205,000 ± 16,000	0.780
NYHA Functional Class (1-5)	2.79±0.48	2.65±0.45	0.550
EUROSCORE	3.54±2.81	2.73±2.32	0.210

Values are presented as n (%) for categorical variables and mean±SD for continuous variables.

MI: Myocardial Infarction, INR: International Normalized Ratio, NYHA: New York Heart Association, BMI: *Body Mass Index, DM: Diabetes Mellitus*

Table 2 Operating information

	Group 1 (n = 72)		Group 2 (n = 46)		p value
	HD (-) (n=68)	HD (+) (n=4)	HD (-) (n=35)	HD (+) (n=11)	0.290
Number of anastomosis	2.2 ± 0.66	2.1 ± 0.71	2.1 ± 0.23	1.92 ± 0.98	0.650
Duration of aortic cross clamp (minutes)	52.3 ± 28.2	54.6 ± 24.3	57.3 ± 16.3	59.4 ± 18.3	0.120
Duration of cardiopulmonary bypass (minutes)	75.5 ± 18.4	80.5 ± 20.6	78.5 ± 19.3	82.5 ± 18.6	0.140
Mean hematocrit value during operation (mg/dl)	8.5 ± 1.05	9.32 ± 1.21	9.17 ± 1.20	8.66 ± 0.76	0.210
Amount of Blood Product Used During Operation (Unit)	1.1 ± 0.2	1.2 ± 0.4	1.0 ± 0.4	1.3 ± 0.8	0.110
Intraoperative glucose level (mg/dl)	196 ± 57	232 ± 59	218 ± 57	174 ± 79	0.510
Use of Inotropic Agent (%)	16 (22.2%)	3 (4.1%)	20 (43.4%)	7 (15.2%)	0.670

HD: Hemodialysis

Table 3 Postoperative data

	Group 1 (n = 72)		Group 2 (n = 46)		p value
	HD (-) (n=68)	HD (+) (n=4)	HD (-) (n=35)	HD (+) (n=11)	
Duration of intubation (hours)	4.2 ± 1.4	4.4 ± 2.5	5.1 ± 1.1	4.3 ± 2.3	0.670
Total drainage volume (ml)	825 ± 273	954 ± 320	754 ± 278	652 ± 445	0.282
Postoperative AF development (%)	11 (15.2%)	1 (1.3%)	8 (17.3%)	3 (6.5%)	0.360
Postoperative blood use (unit)	1.3 ± 0.7	1.8 ± 0.9	1.4 ± 0.4	1.5 ± 0.7	0.641
Pneumonia development (%)	3 (4.1%)	1 (1.3%)	4 (8.6%)	3 (6.5%)	0.04*
Postoperative hemoglobin level (mg/dl)	8.8 ± 1.05	9.5 ± 1.55	7.1 ± 1.22	7.68 ± 0.71	0.028*
Mean duration to drain removal (Day)	2.1 ± 0.5	2.2 ± 1.3	3.0 ± 0.2	2.2 ± 1.2	0.441
Wound infection (%)	1 (1.3%)	2 (2.7%)	3 (6.5%)	2 (4.3%)	0.541
Mean blood glucose level (mg/dL)	132 ± 74	152 ± 56	212 ± 55	184 ± 63	0.321
Duration of intensive care stay (days)	2.2 ± 1.6	6.10 ± 2.3	2.3 ± 2.1	9.1 ± 2.5	0.008*
Duration of hospital stay (days)	8.31 ± 1.2	16.21 ± 3.3	12.5 ± 5.3	19.45 ± 4.3	0.010*
Mortality (%)	2 (2.7%)	1 (1.3%)	2 (4.3%)	2 (4.3%)	0.001*

Hemodialysis patients were 3 males and 1 females in Group 1 and 6 males and 5 females in Group 2. The results of our study did not show a statistically significant relationship between gender and need for postoperative hemodialysis (p=0.398).

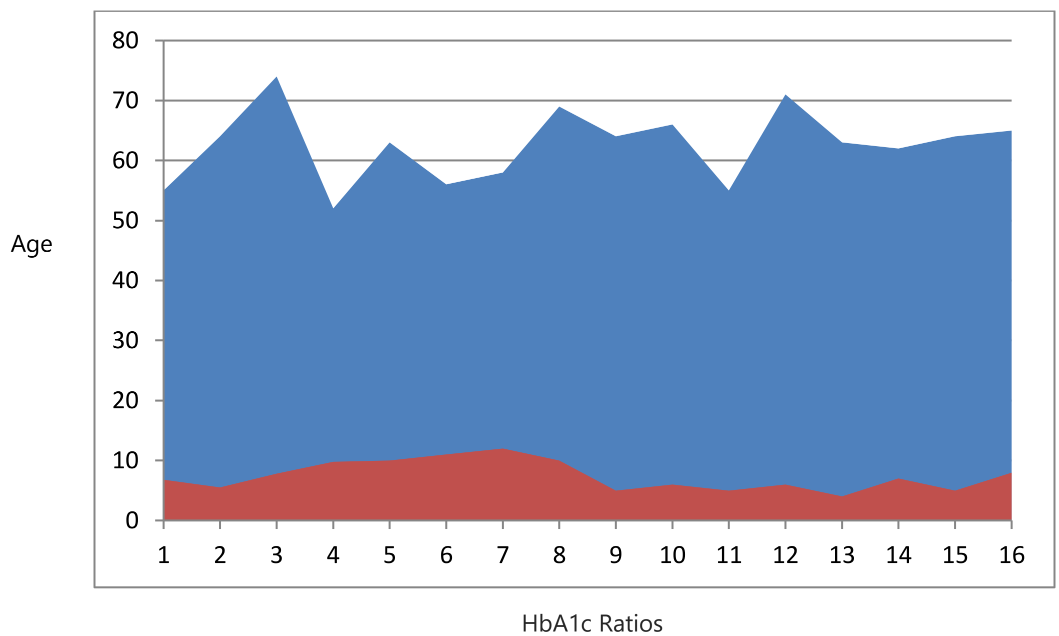

Figure 1 HbA1c ratios according to age distribution

4. DISCUSSION

There are two types of DM: Type 1 diabetes due to insufficiency in insulin secretion and Type 2 diabetes due to insulin resistance Patients with Type 1 DM receive oral antidiabetic treatment while patients with type 2 DM receive subcutaneous insulin therapy. In our study, all patients underwent standard dual insulin therapy, which was started after consulting the internal medicine endocrinology departments. The introduction of standard insulin therapy before major surgery is recommended (American Diabetes Association 2011). In the literature, it is seen that 30-35% of the patients who underwent CABG surgery are composed of diabetic patients (Khot et al., 2003). In our study, 118 of the 295 isolated CABG patients (40%) were diabetic patients. Unlike atherosclerosis, DM causes widespread damage to the vascular endothelium resulting in stenosis and occlusion. As a result, left ventricular function is further impaired in diabetic patients. DM, which causes widespread vascular disease in the body, leads to diabetic nephropathy by causing atherosclerosis in renal arteries and inflammation in glomeruli (Van Dam et al., 2013).

ARF is a condition that is frequently seen after CPB and is mortal if not treated. In CPBG surgery, there are some changes in the body due to exposure to an artificial device after a physiological event (Sanders et al., 2011). Postoperative ARF may be triggered due to many factors such as an inflammatory response induced by the heart-lung machine, hypoperfusion, reperfusion, reheating of blood after hypothermia, and transfusion of blood and blood products. It is known that the risk of ARF is increased especially by the duration of CPB ≥100 min and of aortic cross clamp >65 min (Munir et al., 2013). In a study, Koyner (Koyner et al., 2013) reported that postoperative ARF was developed in 426 (34.9%) of 1219 patients underwent cardiac surgery, which was found to be associated with an increase in length of stay in hospital and intensive care unit and an increase in mortality rate. The mortality rate in our study was found to be 2.3% (n = 7) in 295 patients.

Postoperative acute renal failure was diagnosed according to RIFLE criteria. RIFLE criteria are classified according to the decrease in urine output, increase in urea and creatinine levels and GFR (Glomerular Filtration Rate) within the first 7 days. Hemodialysis was started with classical jugular or femoral venous dialysis catheter after nephrology consultation for our patients. Renal functions can be monitored in the intensive care unit after cardiac surgery by monitoring daily BUN, creatinine and blood gas parameters and hourly urine output. Urine output is one of the best indicators of cardiac performance. However, despite good cardiac performance in diabetic patients, ARF can develop due to glomerular disorders present in the pre-operative chronic period. After the operation, the disorder progresses further and the ARF can develop.

Glycohemoglobin (HbA1c) levels provide information about the mean blood glucose concentration over the last 3-4 months. In the literature, it is suggested that preoperative HbA1c levels should be below 7% (Subramaniam et al., 2014). A study by Halkos (Halkos et al., 2008) on 3555 patients found that the postoperative complication rates were higher in patients with higher HbA1c levels. It was reported that ABR developed in 75 (9.2%) of 814 patients with higher HbA1c levels and 13 cases (1.6%) resulted in mortality. In the same study, it was reported that the risk of postoperative atrial fibrillation (15%) was higher in patients with higher HbA1c levels. In our study, there was a statistically significant increase in mortality rates in the group with higher HbA1c levels ($p < 0.05$).

Glycemic control is very important for diabetic patients in the perioperative and postoperative periods. Therefore, it is recommended that continuous insulin infusion be initiated to achieve glycemic control. A study by Abdulmelak (Abdulmelak et al., 2016) reported a decrease in the rate of mortality and deep sternal infections due to the glycemic control achieved by intraperitoneal insulin perfusion which was continued until the second postoperative day.

In hyperglycemic patients after cardiac surgery, there may be risks such predisposition to infections due to leukocyte dysfunction and delay in wound healing, deep sternal wound infections, deterioration of endothelial functions, and thrombosis due to impaired fibrinolytic activity (Raza et al., 2017). Therefore, the glucose levels of diabetic patients should be closely monitored in the postoperative period (Nagendran et al., 2018). The studies reported different opinions on this subject. In a study conducted by Okabayashi (Okabayashi et al., 2014), it was reported that diabetic patients should have a blood glucose level of 80 to 110 mg/dL. Thus, avoidance of hyperglycemia has been shown to reduce rates of infection and other complications. In contrast, a study by Umpierrez (Umpierrez et al., 2015) reported that the glucose level of diabetic patients should be between 140 and 160 mg/dL, because hypoglycemic attacks have been reported to increase mortality and morbidity during the control of hyperglycemia.

5. CONCLUSION

Many complications can occur after coronary surgery in patients with DM. Therefore, we believe that such patients should be closely monitored and that morbidity and mortality can be reduced considerably. Hemodialysis (HD) may be required after coronary bypass surgery in diabetic patients. Our results showed that the need for hemodialysis was significantly increased in DM patients with higher preoperative HbA1c levels. Although there is no direct correlation between high HbA1c levels and postoperative HD, we

believe that these patients should be more closely monitored with more frequent measurements of urea, creatinine, blood gas and electrolyte levels.

Approval of Ethics Committee

20/06/2018 Date and B.30.2.YYU.0.01.00.00/145

Author Contributions

Concept – Ali Kemal GÜR; Design – Esra Eker; Supervision – Ali Kemal GÜR; Resources and Statistical Analysis – HarunÜnal; Materials – Şahin Şahinalp; Data Collection and/or Processing –Şahin Şahinalp ; Analysis and/or Interpretation - Ali Kemal GÜR; Literature Search – Esra Eker; Yazıyı Yazan / Writing Manuscript - Ali Kemal GÜR; Critical Review Other – Şahin Şahinalp

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